Platelet Glycoprotein IIb/IIIa Inhibitors

To the Editor:

Platelet glycoprotein (GP) IIb/IIIa antagonists only prompt an overall 8.5% relative reduction in 30-day deaths or myocardial infarction in acute coronary syndromes (ACS), and Quinn et al suggested that this limited benefit may be due to factors such as antagonist-induced platelet activation. I suggest that limited benefits of GP IIb/IIIa inhibition are due basically to limited participation of platelets in ACS, although negative effects described by Quinn et al are no doubt operative.

Cases of ACS with and without elevated troponin levels treated by GP IIb/IIIa inhibition provide evidence for a limited role of platelets in ACS. Inhibition in troponin-negative cases was ineffective or slightly worsened ACS, but inhibition in troponin-positive patients yielded a reduction in deaths or infarction of 60% (average of 3 studies). Effects of GP IIb/IIIa inhibition probably define roughly the significant involvement of platelets in ACS, and the striking improvement of only troponin-positive cases provides evidence that platelets are involved significantly only in troponin-positive cases, which comprise about a third (30.9%) of cases of ACS.

A study of abciximab supports significant platelet involvement only in troponin-positive cases. The 6-month risk of death or nonfatal infarction in controls was 23.9% in troponin-positive and 7.9% in troponin-negative cases. Treatment with abciximab did not change the event rate in troponin-negative cases, but reduced the rate in troponin-positive cases to the level of troponin-negative cases.

As platelets are precursors of thromboses, the apparent absence of significant involvement of platelets in troponin-negative cases (about two thirds of ACS cases) raises questions about the validity of the plaque rupture/thromboses mechanism. In contrast, the spasm of resistance vessel (S-RV) concept can explain troponin findings. The concept asserts that symptoms in ischemic heart disease are due to S-RV and, in the minority of cases with significant platelet activation, vasoconstrictive agents from platelets add to S-RV and worsen prognosis.

However, the concept asserts that the major source of S-RV in ACS is stenotic coronary artery disease that causes ischemic injury and consequent ischemia-induced S-RV; a vicious cycle of S-RV, more ischemia, and more ischemia-induced S-RV favors infarction. Plaque rupture, often preexisting, would tend to worsen ischemia and favor platelet activation in some cases. Thromboses are attributed to stasis caused by S-RV–induced no-reflow plus intimal irregularities.

α-adrenergic blockade should be useful in treating ACS. The S-RV concept does give ischemia-induced S-RV the pivotal role in ACS, and ischemia-induced S-RV is reversed by α-adrenergic blockade.

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